

33. The ordered redundant array of claim 30, wherein each extended immobilized oligonucleotide comprises at least 50 copies of said sequence of interest.

REMARKS

Applicants have amended claims 11 and 23 to make explicit that which was implicit. These amendments are supported at page 10, line 9 – page 11, line 6. As such, these amendments do not constitute new matter and their entry is respectfully requested.

Applicants have amended claim 30 to correct certain informalities. Applicants have also amended claim 30 – 33 to make explicit that which was implicit. These amendments are supported at page 10, line 9 – page 11, line 6. As such, these amendments do not constitute new matter and their entry is respectfully requested.

The Examiner objected to certain informalities in claim 30. Applicants respectfully submit that the amendments to the claim have obviated this rejection, and respectfully submit that this rejection should be withdrawn.

Claims 30 – 33 were rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the invention.

Applicants respectfully submit that this rejection be withdrawn for the following reasons.

The Examiner objected to the use of the phrases “extending from each said oligonucleotides along a Z coordinate a plurality of unique circular DNA templates, each circular DNA template comprising a sequence of interest, wherein each said circular DNA template is hybridized to each said oligonucleotides by a region complementary to at least a portion of said sequence of said oligonucleotides” in claim 30.

Applicants respectfully submit that the amendments to these claims have obviated this objection. The array of the present invention has immobilized oligonucleotides at positions on a substrate defined by x and y coordinates. A plurality of sequences of interest which hybridize to the immobilized oligonucleotides in the Z dimension are part of the array. For example, when rolling circle amplification is used to amplify each circular DNA template, the resultant product for each oligonucleotide is a much longer, extended, immobilized oligonucleotide which has repeated

(sometimes referred to as redundant) copies of the sequence of the circular DNA template. Thus, the array, as claimed in claim 30, is a plurality of extended oligonucleotides with at least two copies of a sequence of interest. The amendments to claim 30 make explicit that the final array comprises an ordered redundant array of oligonucleotides. Applicants respectfully submit that these amendments have obviated this rejection, and request its withdrawal.

Accordingly, in view of the foregoing, applicants respectfully submit that all claims comply with 35 U.S.C. § 112, second paragraph.

Claims 11 and 23 were rejected under 35 U.S.C. § 102(b) as being anticipated by Caviani Pease et al.

Applicants respectfully submit that this rejection should be withdrawn for the following reasons.

Unlike arrays such as those taught by Caviani Pease et al., the present array extends in the Z dimension, such that each immobilized oligonucleotide has repeated copies of a sequence of interest. In rejecting claims 11 and 23, the Examiner has taken the position that it is unclear from the claims what is in the array. However, the process used in these claims, as explained in the specification, makes a particular type of array which has repeated sequences of interest in the Z dimension.

As explained above, the ordered redundant array of the present invention is comprised of a series of extended immobilized oligonucleotides which are tethered to a substrate at one end, and extend in the other direction, with repeated copies of the sequence of interest. Applicants respectfully submit that the language of the claims is clear, indicating in particular in step (d) that the product is "an array having at least two copies of said sequence of interest along the z coordinate." However, in order to expedite prosecution, applicants have now amended claims 11 and 23 to even more explicitly point out the composition of the final array product. The product claimed in claim 11 and 23 has at least two copies of a sequence of interest along the Z coordinate, and thus is completely distinguishable from the array described by Caviani Pease et al. Accordingly, applicants respectfully submit that the present invention is not anticipated by Caviani Pease et al., and request that this rejection should be withdrawn.

Claims 11 and 23 were also rejected under 35 U.S.C. § 102(e) as being anticipated by Chetverin et al.

Applicants respectfully submit that this rejection should be withdrawn for the following reasons.

Chetverin et al. does not in any way teach an array wherein there are at least two or three copies and certainly not 10 or 50 copies of the sequence of interest extending in the Z dimension. In issuing this rejection, the Examiner has again alleged that it is unclear from the claims what is in the array. However, as explained above, the process used in the claims makes an array that clearly distinguishes the ordered array of the present invention from the array of Chetverin, which does not teach an ordered redundant array having the recitations cited in claims 11 and 23. Accordingly, applicants respectfully submit that there is no anticipation by Chetverin, and request that this rejection should be withdrawn.

Claims 11 and 23 – 33 were also rejected under 35 U.S.C. § 102(e) as being anticipated by Lizardi et al.

Applicants respectfully submit that this rejection should be withdrawn for the following reasons.

While Lizardi mentions the use of rolling circle amplification and the use of DNA arrays, Lizardi in no way teaches the present array. Lizardi is directed to the detection of specific nucleic acid target molecules in a sample, using rolling circle replication for detection of these target sequences. There are clear physical distinctions between array of Lizardi and the array of the present invention. In Lizardi, the nucleic acid array consists of immobilized target probes or detection probes, unligated and unextended. In order to use this array to detect the presence of a specific target in a sample, the sample is exposed to the array, and any sample molecules which hybridize to the immobilized target probes are amplified using rolling circle amplification. Thus, in Lizardi, the DNA ligation and extension (amplification) steps are used to determine the presence of the target DNA in solution, such that the amount of DNA amplification is proportional to the concentration of the target DNA present in the sample.

In other words, the Lizardi does not anticipate the present invention, because each immobilized probe is present only once in the Z dimension of the Lizardi array, rather than repeated as it is in the present array.

The Lizardi array after its use in sample detection does not anticipate the present invention, because not every immobilized probe will be amplified because not every probe will hybridize to a target nucleic acid in the sample. Thus, the Lizardi array after its use in sample

detection has **varying** amounts of amplified DNA present at different positions on the array, including many positions which are not amplified. In contrast, it is clear from the claims and the specification that **each** immobilized oligonucleotide in the present array contains at least two copies of the sequence of interest. Thus, **all** of the oligonucleotides at each position on the present array are amplified, e.g., 1,000 copies of the target, and what is claimed is the product **after** DNA amplification.

Moreover, Lizardi does not teach any advantage or utility for such an ordered redundant array, as taught by the present invention. Accordingly, applicants respectfully submit that this rejection should be withdrawn.

As such, the rejection of these claims under 35 U.S.C. § 102(e) should be withdrawn.

In view of the foregoing, Applicants respectfully submit that all claims are in condition for allowance. Early and favorable action is requested.

Respectfully submitted,



Ronald I. Eisenstein
Reg. No. 30,628
Nicole L. M. Valtz
Reg. No. 47,150
Nixon Peabody LLP
101 Federal Street
Boston, MA 02110
617.345.6054

Date March 6, 2003.

Customer No. 26248

APPENDIX

The changes made by the amendments to the claims are shown below, with insertions being underlined and deletions being bracketed.

11. (amended) An ordered redundant array of immobilized oligonucleotides produced by:

(a) providing: i) a solid support comprising a plurality of positions for oligonucleotides, said positions defined by x and y coordinates; ii) a plurality of identical oligonucleotides, each oligonucleotide comprising a sequence; and iii) a plurality of unique circular DNA templates, each circular DNA template comprising a sequence of interest and a region complementary to at least a portion of said sequence of said oligonucleotides, said sequence of interest being different for each circular template;

(b) immobilizing one oligonucleotide from said plurality of identical oligonucleotides in each of said positions on said solid support to create an ordered array comprising a plurality of identical immobilized oligonucleotides;

(c) adding to each immobilized oligonucleotide of said ordered array a circular DNA template from said plurality of said unique circular DNA templates under conditions such that said immobilized oligonucleotide hybridizes to said circular DNA template to create a plurality of primed circular templates, each primed circular template comprising a different sequence of interest; and

(d) extending each of said primed circular templates along a z coordinate to create an extended immobilized oligonucleotide comprising at least two copies of said sequence of interest, thereby generating an ordered redundant array of extended immobilized oligonucleotides, wherein said ordered redundant array refers to said array having each extended immobilized oligonucleotide comprise at least two copies of said sequence of interest along the z coordinate.

23. (amended) An ordered redundant array of immobilized oligonucleotides produced by:

a) providing: i) a solid support comprising positions for oligonucleotides, said positions defined by x and y coordinates; ii) a plurality of oligonucleotides, each oligonucleotide comprising a sequence complementary to a different portion of the sequence of said target nucleic acid; and iii) a plurality of corresponding circular DNA templates, each circular DNA template comprising a different portion of the sequence of said target;

b) immobilizing each of said oligonucleotides in one of said positions on said solid support to create an ordered array comprising a plurality of immobilized oligonucleotides;

c) adding to each immobilized oligonucleotide of said ordered array along a z coordinate a corresponding circular DNA template under conditions such that said immobilized oligonucleotide hybridizes to said corresponding circular DNA template to create a plurality of primed circular templates; and

d) extending said primed circular templates to create an ordered redundant array of extended immobilized oligonucleotides, each extended immobilized oligonucleotide comprising at least two copies of said portion of said sequence of said target nucleic acid, wherein said ordered redundant array refers to said array having each extended immobilized oligonucleotide comprise at least two copies along the z coordinate of said portion of the sequence of interest contained in said primed circular template.

30. (amended) An ordered redundant array of immobilized oligonucleotides comprising:

a solid support comprising a substrate, wherein said substrate contains i) a plurality of positions for oligonucleotides, said positions defined by x and y coordinates; and ii) a plurality of [identical] extended oligonucleotides immobilized on the substrate which extend into the z coordinate, wherein each extended immobilized oligonucleotide comprises a sequence of interest, [; and iii) extending from each said oligonucleotides along a z coordinate a plurality of unique circular DNA templates, each circular DNA template comprising a sequence of interest, wherein each said circular DNA template is hybridized to each said oligonucleotides by a region complementary to at least a portion of said sequence of said oligonucleotides, and wherein said sequence of interest is different for each circular template,] wherein each sequence of interest is different for each extended immobilized oligonucleotide and corresponds to a portion of a target, and wherein each extended immobilized oligonucleotide comprises [said circular template

creates an extended immobilized oligonucleotide comprising] at least two copies of said sequence of interest such that the array has redundancy in the z-dimension.

31. (amended) The ordered redundant array of claim 30, wherein [said circular template creates an] each extended immobilized oligonucleotide comprises [comprising] at least three copies of said sequence of interest.

32. (amended) The ordered redundant array of claim 30, wherein [said circular template creates an] each extended immobilized oligonucleotide comprises [comprising] at least 10 copies of said sequence of interest.

33. (amended) The ordered redundant array of claim 30, wherein [said circular template creates an] each extended immobilized oligonucleotide comprises [comprising] at least 50 copies of said sequence of interest.